PEER REVIEW HISTORY

BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form (**http://bmjopen.bmj.com/site/about/resources/checklist.pdf**) and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below.

ARTICLE DETAILS

TITLE (PROVISIONAL)	Efficacy of phototherapy to treat facial aging when using a red versus amber LED: a protocol for a randomized controlled trial
AUTHORS	Rocha-Mota, Lidiane; Motta, Lara; Duarte, Ivone; Horliana, Anna Carolina; Silva, Daniela; Pavani, Christiane

VERSION 1 – REVIEW

REVIEWER	Motoki Nakamura Department of Geriatric and Environmental Dermatology, Nagoya City University Graduate School of Medical Sciences, Nagoya, Japan
REVIEW RETURNED	13-Feb-2018

GENERAL COMMENTS	The study protocol entitled “Efficacy of phototherapy to treat facial aging when using a red versus amber LED: a protocol for a randomized controlled trial” by Rocha Mota L. et al is a randomized, double-blind, split-face clinical trial to evaluate the cosmetic efficacy of red and amber visible light. Red visible light is widely known as the wavelength having good aesthetic effects and amber visible light is also promising. This protocol is well designed and valuable results can be expected. Following points should be addressed. Sometimes skin aging of the face shows big laterality. Unilateral sun exposure is considered as the main reason and it occurs when people drive cars for long time, every day. So they should exclude people having big laterality of skin aging on their face and professional drivers.

REVIEWER	LUIS TOREZAN HOSPITAL DAS CLINICAS UNIVERSITY OF SAO PAULO BRAZIL
REVIEW RETURNED	14-Feb-2018

GENERAL COMMENTS	The study seems to be well-designed, but i have some issues to be discussed and sugest review: - LEDs are used in medical literature not only for aesthetics but for wound healing. - Page5 - at the end" In Brazil, the companies..." This is not suppported by literature and appears to have commercial bias (to the reader). I suggest to rmove th whol paragraph. Sudy design: I did not understand why the authors suggest to treat both groups with both LEDs making a reassessment at day 180. You could make an intra individual evaluation and compare the efficacy

	of 2 diferent wavelenghs. How do you proceed with patients during the long f-u? Will they apply mosturizers or any SPF fator. Of course this is an importante issue once it will modify the wrinkle volume Elasticity and sagging: " cutaneous elasticity is an important..." It provides" Indirect" information on the quality... Why do not include skin type I? Justify. Please switch "pathologies" for " skin diseases" Any dermatologist participating in the study? Or at least evaluating the patients`including and excluding criteria. This is an important question.

VERSION 1 – AUTHOR RESPONSE

Point-by-point answer to Reviewer(s)' Comments:
*** Editor Comments to Author:
- Please ensure that the information provided in the trial registry is consistent with your protocol article. For example, the trial registry states that the target sample size for the trial is 40 participants, whereas in your protocol you calculate the required sample size to be 137. Please update the registry record accordingly.
We are updating the trial registry. Since at the beginning we did not have robust trials to base on, in order to make the sample size calculation, the ethics approval and registry were based upon 40 participants. After a pilot study with 10 participants, we sample size calculation was performed and this protocol article was submitted. A project amendment was approved by the ethics committee of this university rising the number of participants, the trial registry is under updating.
*** Referee 1 Comments to Author:
The study protocol entitled “Efficacy of phototherapy to treat facial aging when using a red versus amber LED: a protocol for a randomized controlled trial” by Rocha Mota L. et al is a randomized, double-blind, split-face clinical trial to evaluate the cosmetic efficacy of red and amber visible light. Red visible light is widely known as the wavelength having good aesthetic effects and amber visible light is also promising. This protocol is well designed and valuable results can be expected.
We thank the reviewer for the careful analysis of our work and we are grateful for the positive evaluation.
Following points should be addressed.
Sometimes skin aging of the face shows big laterality. Unilateral sun exposure is considered as the main reason and it occurs when people drive cars for long time, every day. So they should exclude people having big laterality of skin aging on their face and professional drivers.
We thank the reviewer for this very important point. Big laterality of skin aging on the face and professional drivers were included as exclusion criteria of this study (Section Methods and Analysis, Exclusion Criteria, Page 7).
*** Referee 2 Comments to Author:
The study seems to be well-designed, but I have some issues to be discussed and suggest review:
- LEDs are used in medical literature not only for aesthetics but for wound healing.
We thank the reviewer for the careful analysis of our work and we are grateful for the positive evaluation. We agree that the literature is huge regarding in the LEDs use in wound healing and is recent the aesthetics application. This information was inserted within the text. (Section Discussion, Page 11).
- Page5 - at the end" In Brazil, the companies..." This is not suppported by literature and appears to have commercial bias (to the reader). I suggest to rmove th whol paragraph.
As suggested by the reviewer this paragraph was removed from the manuscript.
Study design: I did not understand why the authors suggest to treat both groups with both LEDs making a reassessment at day 180. You could make an intra individual evaluation and compare the efficacy of 2 diferent wavelenghs.

The main objective of this study is to make this intra individual evaluation of the efficacy of the two different wavelengths, as pointed by the reviewer. However, once the treatments may not present the same efficacy, it is ethical to provide the cross-treatment to the participant. Since we are going to make this, we decided to evaluate the participant after the 180 days and verify if the effects of the first treatment would disappear after this washout period and if the clinical response to the second treatment would be different from the first one (Section Methods and Analysis, Interventions, Page 9).

How do you proceed with patients during the long f-u? Will they apply mosturizers or any SPF fator. Of course this is an importante issue once it will modify the wrinkle volume.

At the beginning of the study, the participants will receive information regarding the importance of the use of sunscreen on skin health, preventing skin cancer and wrinkles. The participants will inform at the anamnesis questionnaire (at baseline and after the 180 days follow up) their habits in terms of sun exposure and use of facial cosmetics and solar filters. These data are going to be used in statistical analysis in order to verify the effect of the use of solar filters in the results obtained. (Section Methods and Analysis, Study Design, Page 6).

Elasticity and sagging: " cutaneous elasticity is an important..." It provides" Indirect" information on the quality...

As suggested by the reviewer the word “indirect” was included in the statement. (Section Methods and Analysis, Variables of the study, Page 10).

Why do not include skin type I? Justify.

It is known that melanin absorbs light in the visible and infrared region of the spectra. We believe that the results of the application of both LED, in the red and amber, may be affected by the melanin content of the skin. In this sense, skin types II, III and IV were chosen as inclusion criteria in a way to standardize the melanin content of the participants, excluding the skin types with high melanin content (types V and VI) and the lower melanin content (Type I). (Section Discussion, Page 12).

Please switch "pathologies" for " skin diseases"

As suggested by the reviewer the word “pathologies” was changed to “skin diseases". (Section Discussion, Page 12).

Any dermatologist participating in the study? Or at least evaluating the patients` including and excluding criteria. This is an important question.

The reviewer raised an important question. The medical doctor ISD, author of this study, will perform the skin evaluation during the screening of patients. She has also participated of the study design. All the treatment and evaluation procedures during the study will be performed by beauticians, since the procedures are noninvasive they are included in beauticians professional attributions. In case of the participants present any complication, ISD will evaluate the participant and guide the treatment. (Section Methods and Analysis, Study Design, Page 6 and Discussion, Page 13).

VERSION 2 – REVIEW

REVIEWER	Motoki Nakamura Nagoya City University, Japan
REVIEW RETURNED	29-Mar-2018

GENERAL COMMENTS	All the points I have mentioned were corrected appropriately.

VERSION 2 – AUTHOR RESPONSE

Point-by-point answer to Reviewer(s)' Comments:

*** Editor Comments to Author:

- We noted that you have now included the anamnesis questionnaire in your methods section in

response to the reviewers comments. Please include some additional information regarding the anamnesis questionnaire for readers who are not familiar with it. Furthermore, please confirm whether the questionnaire been validated in Brazil? If so, please include the citation to the published questionnaire validation.
We thank the editor for the careful analysis of our work. We included the following information regarding anamnesis: “After recruitment, the researcher will check if the patient meets inclusion/exclusion criteria based on anamnesis and skin evaluation. Anamnesis is an interview performed by the health professional in order to know the patient medical and aesthetics treatment history, as well as daily personal and social habits. Regarding the daily personal and social habits, anamnesis will include information regarding sun exposure, smoking and drinking frequency, sleep quality, food and water intake, professional aesthetics treatment on the face and homecare cosmetics use. Anamnesis was not validated since it is not an instrument to measure patient outcome. Skin evaluation, which will be performed by a medical doctor (ISD), includes skin phototype and degree of wrinkles severity”. (Methods and Analysis Section, Study Design, page 6).
- Please update your article in relation to the current recruitment status. You sate in your methods that "The study will last for 2 years, with a start date of April 2018. The study is not recruiting yet." As it is now April 2018 can you clarify whether recruitment has already commenced? Please update this statement accordingly. If recruitment has commenced then please also update the last sentence of your abstract to reflect this.
Since this study protocol is not published yet, we delayed the stating date for recruitment. The study will have a start date of May 2018 (Methods and Analysis Section, Study Design, page 6).
- Please ensure that you improve the quality of language in your manuscript, either with the assistance
of an English-speaking colleague or with a professional copyediting agency.
We have had the manuscript revised by a copyediting agency and the certificate was attached .
*** Reviewer(s)' Comments to Author:
Reviewer: 1
All the points I have mentioned were corrected appropriately.
We thank the reviewer for the careful analysis of our work and we are grateful for the positive evaluation.